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Medicais: Intelligent Prediction of Medication Non-Adherence and Intervention System

Julius M. Sunday[1], Alo U. Rita[2], Onu F. Uchenna[3], Akobundu C. Ihuoma[4], Nwani H. Ogbu[5] and Eze F. Chukwuka[6]

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Abstract: patient's non-adherence to medication has been widely recognized as one of the major problems in healthcare domain worldwide. The prevalent of the problem and its great consequences call for a combined effort towards the development of efficient adherence intervention system. in this study, development of web based intelligent prediction of patient's non-adherence to medication and intervention system called imedicais was proposed to improve medication adherence. with imedicais, three independent sub-systems consist of anfis predictive model, assessment of medication non-adherence level and adherence intervention were integrated for prediction of non-adherent patients, evaluation of medication non-adherence level with its causes and delivery of personalized persuasive messages to individual patient respectively. outpatients' non-clinical dataset of 609 records was generated through a validated questionnaire-based survey administered at three tertiary healthcare centres in the south east region of nigeria for the training and testing of the anfis predictive model. for the computation of patient's adherence level and other factors that influence non-adherence, an emulator sub-system was design. knowing the patient's level of non-adherence and the factors that influence it either by prediction or assessment, the system send personalized persuasive messages to the patient as intervention towards improving medication adherence. the intelligent web-based application with integration of sms, ussd and agent voice call api were implemented using visual studio dot net framework, matlab r2020a programming language, twilio and africa's talking apis and other web services. the proposed system could greatly improve patient's adherence to medication as it has the potential to accurately identify patients who are unlikely to adhere to their prescribed medication with likely causes of their non-adherence and deliver an appropriate persuasive message that can influence medication adherence behavior.

Keywords: *adherence intervention, ANFIS prediction, medication non-adherence, patient's non-clinical dataset,*

1. Introduction

Medication non-adherence has been widely recognized as one of the major prevalent problems in healthcare domain worldwide [1-2]. It is associated with multidimensional consequences that threaten clinical and therapeutic success especially among the outpatients with chronic illnesses irrespective of the disease class. Studies on prevalence of medication non-adherence and its associated factors among patients with chronic diseases such tuberculosis, cancer, HIV/AID, mental disorder, diabetes have been widely established. The far-reaching consequences of medication non-adherence on healthcare system and society call for a multifaceted approach. Such consequences leading to prolong treatment duration, medication wastage, high healthcare cost and even increased mortality [3-4]. Leveraging machine learning algorithms to accurately predict patients who are unlikely to adhere to their prescribed medication is highly essential and could be used to drive an efficient patient-centric adherence intervention. Over the years, several systems have been developed to address the multifactorial problem of medication non-adherence among outpatients using different approaches. For example some studies [5-10] focused on assessment of medication non-adherence and various factors that influence patients' non-adherence to medication. The commonly used tools include but not limited to self-report questionnaire (Morisky adherence scale, brief medication questionnaire and hill-bone compliance scale), therapeutic drug monitoring, electronic medication monitoring devices, pick-up or refill-rate and so on [11-13]. This kind of approach could only

[1] *Evangel University Akaeze, Nigeria*
ORCID ID : 0000-0002-4569-9121
[2] *Alex Ekwueme Federal University Ndufu Alike, Nigeria*
[3] *Ebonyi State University Abakaliki, Nigeria*
** Corresponding Author Email: Julius.michael@evangeluniversity.edu.ng*

establish whether medication non-adherence is prevalent or not in a sample population and to determine if prevalent or not-prevalent what are the factors responsible. For assessment of medication non-adherence, there are universal standards available especially for indirect patient self-reported method using questionnaire. The mostly used is Morisky adherence rating scale of 8-items but it can only be applied for patients who have been on medication for about two months. However, factors that influence non-adherence cannot be efficiently determined with the assessment systems, hence iMedicaIS: Intelligent Prediction of Medication Non-Adherence and Intervention System which is a proposed system in this research that could greatly improve patient's adherence to medication as it has the potential to accurately identify patient who are unlikely to adhere to their prescribed medication with likely causes of their non-adherence and deliver an appropriate persuasive message the can influence medication adherence behaviour

2. Related Literature

Most studies in [14-19] centred on intervention to improve medication adherence using multidisciplinary strategies such as theory based intervention; medication packaging based intervention, risk communication based intervention, self-management intervention, educational/literacy based intervention, integrated care based intervention and emerging technology based intervention. The main objective of the adherence intervention is to establish a deliberate process or act tailored towards improving medication adherence and reducing non-adherence to medication. Intended outcome is to ensure both intentional and unintentional causes of non-adherence are addressed through simplification of dosing regimens, reminder, communication between caregiver and patient. In most studies, technology delivery tools of adherence intervention functions (messages) to improve adherence are limited to via mobile phone technology and services such as short message service (SMS) and phone calls which are not efficient. Contents of the adherence messages are usually generic, monolingual and not persuasive. Thus, leading to alert fatigue, alert override and message irrelevance. Also, it has been observed that many of these studies on adherence intervention failed to take into consideration the patient's medication adherence assessment before the design and deployment of adherence intervention strategy. Adherence interventions without leveraging adherence assessment outcomes or prediction results oftentimes yield little or no desired result. However, recently in some studies [20-25], integration of persuasive technology with various medication adherence intervention system has emerged as new proactive approach to enhance adherence intervention for improving medication adherence through the delivery of persuasive and personalized messages. Persuasive systems are usually designed to interactively foster change in people's attitude, perception, knowledge and behavior or promote patients' health behavior without necessarily pressurizing them [20, 21]. The study in [20], summarized the common platforms created and deployed for persuasive systems in healthcare intervention to include ambient and public display, sensor and wearable device, desktop and other specialized devices, web and social network, game and mobile and hand-held devices. For effective and efficient delivery of persuasive messages aimed to change human behavior, attitude, perception and others from bad to good, good to better, an appropriate persuasive strategies and principles must be adopted in the design and development of such systems. In [25] six layers of principles of persuasiveness was developed which are reciprocity, commitment, consistency, social proof, liking and scarcity. Following the increasing use of mobile phones among the healthcare stakeholders and application of IoT devices in healthcare, persuasive mobile application can be designed and integrated into intervention system to improve medication adherence.

The last approach in a bid to improve patients' adherence to medication, the use of machine learning algorithms on clinical and non-clinical patients' dataset to predict patients who are unlikely to adhere to their prescribe medications and to identify the factors that could be responsible for their non-adherence is at increase. Several studies by [26-36], have successfully applied machine learning predictive algorithms/models in the domain of medication adherence. These predictive algorithms include Super Vector Machine (SVM); Long Short Memory (LSM) Network; back propagation neural network; radia basis function; statistics logistic regression; discriminant analysis; information gain; random forest; adaptive neuro-fuzzy and so on. Many of these predictive models have been used for risk prediction in patients with coronary heart and cardiovascular diseases [36], prediction of emergency department services in hospital [37], prediction of chronic kidney disease progression [38], development of fuzzy based diagnostic agent [39], intelligent hepatitis diagnosis [28], prediction in medicine and healthcare [31], application of neuro-fuzzy in healthcare, genetic fuzzy logic healthcare data classification, predicting survivability of cancer patients, estimating mental states of a depressed persons, machine learning precision psychiatry [32], prediction of weight changes in chronic schizophrenic patients, etc. Also, machine learning techniques have been used for identification of factors that cause health challenges, issues, diseases and ill health in the domain of healthcare. For examples, studies in [30, 40] used random forest algorithm to evaluate the influence of demographic data on causes of coronary artery disease. However, these systems have been inefficient and sub-optimal in performance due to: inaccurate identification of non-adherent patients, failure to detect the causes of medication non-adherence in individual patient and vagueness and delivery of generic rather than personalized intervention messages.

With plethora studies reviewed in relation to machine learning prediction of patient non-adherence to medication and intervention system, the research/knowledge gaps found are categorized into three groups namely, (1) assessment of medication non-adherence (2) prediction of medication non-adherence using machine learning algorithms and (3) intervention to improve medication adherence.

In order to effectively and efficiently address the problem of medication non-adherence and improve patient's adherence to medication, this research aimed at development of intelligent machine learning prediction of patient's non-adherence to medication and intervention system. The specific study objectives are to: (i) generate non-clinical dataset on medication non-adherence using cross-sectional survey for the machine learning predictive and adherence intervention system. (ii) determine and select from the generated dataset the most relevant features (factors) that influence medication non-adherence as inputs to the predictive system using correlation and sensitivity algorithms. (iii) design adaptive neuro-fuzzy inference system (ANFIS) for prediction of patient's medication non-adherence level (iv) develop a web-based application with integrated SMS, agent voice call and USSD App for medication non-adherence prediction and assessment, medication prescription, booking of next clinical appointment, composition and delivery of personalized persuasive messages as adherence intervention to improve medication adherence (v) evaluate the system's performance using real world data and carry out comparative analysis with the related existing systems.

3. Methodology

Development of machine learning prediction of patient's medication non-adherence and intervention system, due to its multidisciplinary nature, hybrid methodology is adopted for the three phases of this study which are:

i. Data and information gathering phase (dataset creation) using quantitative and qualitative methods (mixed)

ii. Software development phase using object-oriented analysis and design (OOAD) with rapid application development (RAD).

iii. System performance and user's satisfaction evaluation phase (experiment and quantitative methods)

3.1 Data Acquisition and Data Pre-Processing

Data were gathered from different levels of stakeholders in three tertiary healthcare centers in southeast region, Nigeria, among professional psychologist and information technologists through the use of semi-structured interview and validated questionnaire.

Cross-sectional survey questionnaire was distributed to 609 outpatients with non-communicable chronic diseases across three (3) tertiary healthcare facilities in the southeast region of Nigeria. The facilities include Alex Ekwueme Federal University Teaching Hospital Abakaliki, Ebonyi State; Federal Medical Centre Umuahia, Abia State; and Federal Medical Centre Owerri, Imo State. The dataset contains data on demographics, medication regimens, use of USSD code, an agent's voice call with SMS to deliver persuasive adherence intervention messages, and reasons for missing medications. Also, generated data on attitude, medication belief, and disease knowledge of patients towards medication non-adherence were assessed by a likert scale of 4-point and 5-point for categorization. The collated data formed the multi-dimensional datasets. Leveraging patients' multi-dimensional datasets advanced the course of improving patient's medication adherence in the following ways to; (1) assess patient's level of knowledge, behavioral pattern, belief, perception and medication non-adherence; (2) determine the correlation that exist among patient's related factors that influence non-adherence to medication such as knowledge, belief, perception, and behavioral pattern; (3) assess and establish patient's need for adherence intervention tool and (4) evaluate patient's intention to use mhealth to improve adherence (5) develop ANFIS prediction model for patient's non-adherence to medication .

The questionnaires consist of four parts: Socio-demographic characteristics: gender, age, marital status, religion, education, occupation, nature of occupation, caregiver and preferred language. The part one (1) also include the type of location address, type of phone, phone usage level in sending and receiving text messages and calls and current health disease name. Part two (2) of the questionnaire has eight (8) different sub-sections consisting of medication taking details; medication adherence assessment, patient attitude, patient belief, patient perception, patient knowledge, intervention needs and suitability and sustainability of the intervention. The collected dataset was not only used to train and test the ANFIS predictive model but also used for analysis of identified factors that influence medication non-adherence. The dataset with the questionnaire has been published and can be accessed online in [1]

3.2 Feature Selection Using Correlation Method Analytic Hierarchical Process (AHP)

AHP is one of the multi-criteria decision analysis models that can be used to compare alternatives/criteria with reference to specify criterion in a pair wise manner and resulting final comparison matrix may be utilized to evaluate and rank alternatives to help in decision making process [41]. As a mathematical validated tool, it uses a hierarchical structure to present a complex decision problem by decomposing it into smaller sub problem. It has been extensively used to identify, evaluate and rank critical and success factors for the design and development of construction project, software project, manufacturing, health intervention project and so on especially multi-criteria and multi-factor ones [42]. Considering the multiple intertwined factors that influence medication non-adherence, using AHP to identify, evaluate and rank the most influencing factors for the analysis so as to guide in the design of patient centric healthcare assistive medication adherence intervention system is inevitable. The under-listed steps describe the model formulation.

i. Developed structure that defines the goal of identification, evaluation and ranking of critical factors for the design of patient centric medication adherence intervention system.

ii. From the literature reviewed, the identified factors are categorized into seven (7) main factors and the hierarchy structure of their sub-factors is provided.

iii. The main factors and sub-factors are differently ranked based on their attribute in a simple method of pairwise comparison matrices by expert judgment based on the survey questionnaire using AHP.

iv. Consistency of the expert judgment is evaluated to a known healthcare whether the judgement is reasonably or unreasonably consistent.

The outcomes of the ranking of the factors formed the choice of input parameters and variables that are fed into the adaptive neuro-fuzzy predictive mode for prediction. The most relevant and essential features are four (4) input variables which are assessment score of patient's belief on medication (PBM), assessment score of patient's behavioural pattern (PBP), assessment score of patient's knowledge on medication with disease (PKM) and assessment score of patient's perception towards prescription and general medical advice (PPP).

4. Description and Design of Proposed iMedicaIS

The prevalent of medication non-adherence among outpatient is a multifactorial problem in public health domain [2] and it requires a multifaceted approach for solution. Proposed iMedicaIS, machine learning prediction of patient medication non-adherence and intervention system is an hybrid system that integrate three independent sub-systems working together in order to achieve the research aim and its specific objectives. The proposed system consists of Adaptive Neuro-Fuzzy Inference System (ANFIS) for prediction, assessment system for medication non-adherence level of patients and adherence intervention system. While ANFIS is used as an intelligent prognosis tool to assist healthcare providers to predict medication non-adherence level of patient visiting clinic for the first time (new patient), assessment system is used to determine the level of medication non-adherence of outpatients (regular) who have been visiting clinic at intervals to receive their medication. The adherence intervention system is concerned with delivery of persuasive personalized messages of different contents depending on the purpose to be achieved in individual patient's treatment need based on their predicted or assessment result. By integrating the Adaptive Neuro Fuzzy Inference System (ANFIS) and assessment of medication non-adherence system with adherence intervention system is to enhance the performance and robustness of the existing system by adding intelligence and accurate predictive capability in improving patient level of adherence to medication. Figure 1 is the conceptual framework of the iMedicaIS.

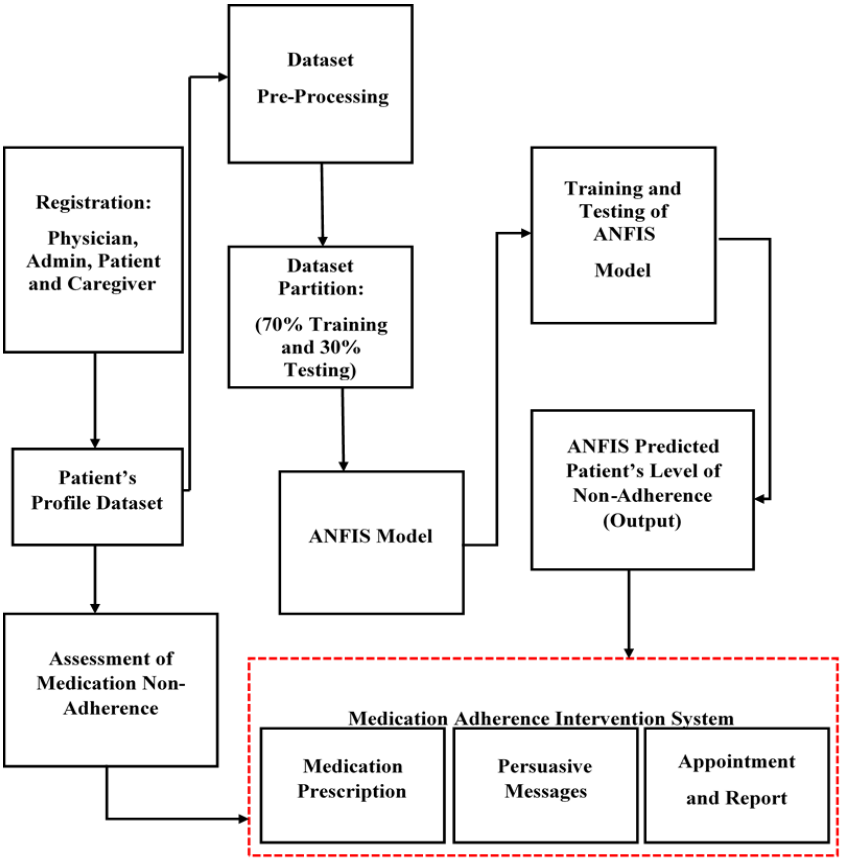

Figure 1. Conceptual framework of the proposed system iMedicaIS

4.1 Design of the ANFIS Predictive Model

ANFIS predictive model is a learner network equivalent to the Takagi-Sugeno fuzzy inference system [43]. Its FIS component consists of five (5) stages which are fuzzification, a knowledge base, a defuzzification, and a decision making. ANFIS learns through the continuous update of the network inputs with factors of layer 1 to 4 as the learner type. Factors of the first layer determine membership functions while factors layer 4 determine the first order estimated functions. Prediction capability of ANFIS is as a result of being a hybrid system of Neural Network and Fuzzy logic which make it better than any single machine learning algorithm.

In figure 2, a typical structure or architecture of ANF predictive model is depicted and it has five (5) basic layers which are:

i. Fuzzification of input and output variables membership function layer: The first layer is generally referred to as fuzzification stage where input variables and output variable are identified and converted to fuzzy variables in linguistic terms as membership functions. The fuzzification of the input variables in form of linguistic term being calculated

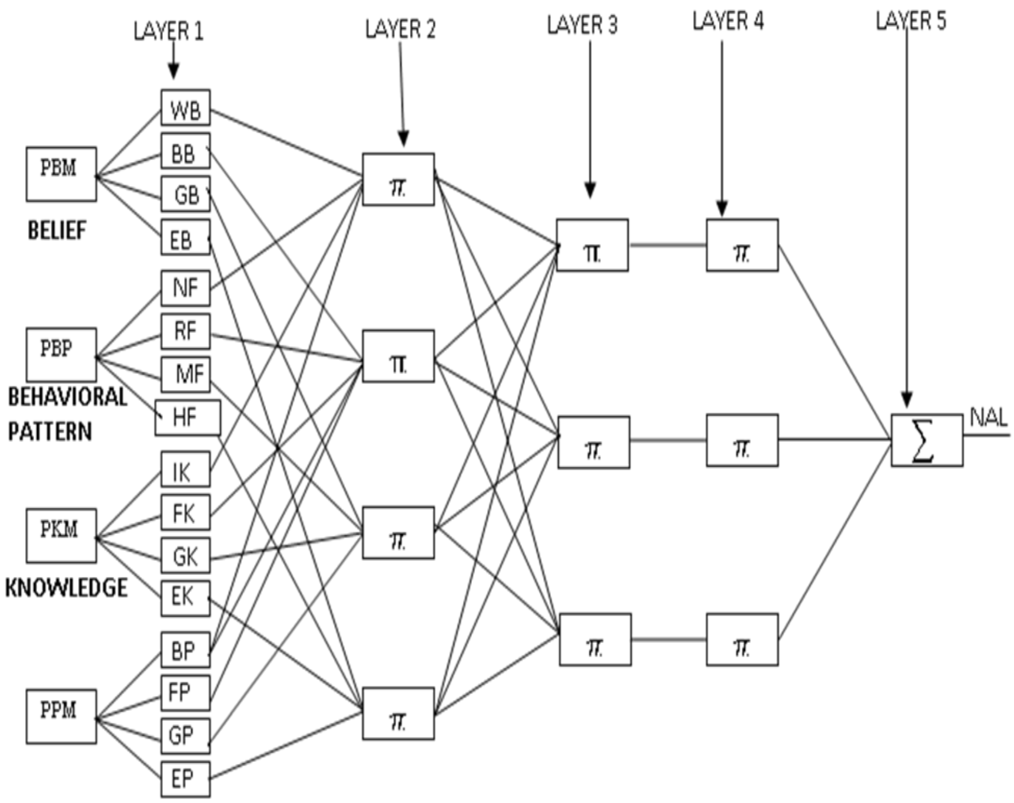

Figure 2. Design ANFIS architecture for Predictive Model of 4 inputs with 4 linguistic terms

based on the premise of each fuzzy rule such as variable PBM (i.e patient belief on medication and disease) is fuzzified into negative, fair, good and excellent belief. The computing units are referred to as nodes. Each input node in the fuzzification stage is an adaptive node.

ii. Multiplication layer: This layer is called second layer of stage two where each node represents a rule and the product of the nodes are calculated.

iii. Normalization layer: The normalized value of the product of each rule generated in the layer two is computed and the result which is the output of the layer 3 is also normalized.

iv. Fuzzy inference or consequent layer: This known as layer four where the output of each neuron is computed by the normalized output of the layer three and by the degree of activation of the consequent of the rule.

v. Defuzzification or summation layer: In the fifth rule, the summation of all the outputs from the layer four is computed and the weighted average of the consequent rules in the layer four is generated.

In the proposed ANFIS predictive model, the design ANFIS architecture is shown in figure 2. There are four (4) input variables which are assessment score of patient's belief on medication (PBM), assessment score of patient's behavioural pattern (PBP), assessment score of patient's knowledge on medication with disease (PKM) and assessment score of patient's perception towards prescription and general medical advice (PPP) with four (4) linguistic terms for each input variables as shown in the figure2

The four (4) linguistic terms for each of the input variables are expressed as follow:

i. Patient's perception towards medication and medical advice (PPP) has:

1. Bad perception (BP)

2. Fair perception (FP)

3. Good perception (GP)

4. Excellent perception (EP)

ii. Patient's behavioural pattern (PBP) has:

1. Not forgetful (NF)

2. Rarely forgetful (RF)

3. Moderately forgetful (MF)

4. Highly forgetful (HF)

iii. Patient's belief on medication (PBM) has:

1. Worse belief (WB)

2. Bad belief (BB)

3. Good belief (GB)

4. Excellent belief (EB)

iv. Patient's knowledge on medication and disease (PKM) has:

1. Inadequate knowledge (IK)

2. Fair knowledge (FK)

3. Good knowledge (GK)

4. Excellent knowledge (EK)

v. Patient's non-adherence level (PNAL) as output has:

1. Very low non-adherence (VLNA)

2. Low non-adherence (LNA)

3. High non-adherence (HNA)

4. Very high non-adherence (VHNA)

The ANFIS architectures in figure 2, has only one (1) output variable that is being generated from four (4) input variables with 4 linguistic terms for both inputs and output for better classification

4.2 Assessment of Medication Non-Adherence Level Sub-System

Assessment of medication non-adherence level is a sub-system of the proposed web-based iMedicais application. It takes into consideration the necessity of assessing the medication non-adherence level of patients prior to the delivery of any persuasive messages via SMS and agent voice call as intervention aimed at improving patient adherence to medication. There are four major patient's related factors that influenced medication non-adherence that were captured via the survey questions and assessed. These include patient's level of knowledge on medication knowledge, patient's level of belief towards the medication and disease, patient's behavioural pattern, patient's perception and also medication non-adherence assessment.

For assessing the medication non-adherence level of patient, Morisky Medication Adherence Rating Scale Questionnaire is adopted. Regular outpatients are presented with Morisky adherence assessment form using rating scale of 8-item questions to respond to and upon the submission, the responses are scored. The cumulative scores for each patient is classified and interpreted as follows: The medication non-adherence questions are scored by response order: 0 score for correct response "No" and 1 for incorrect response "Yes" applicable to all the questions except the fifth question which is in the reverse order and the last question where only the option "A" response is scored 0 while option "B-E" is scored 1. The cumulative scores (CS) of non-adherence level is calculated and categorized as follow: CS 6-8 means very high non-adherence, CS 4-5 means high non-adherence, CS 2-3 means low non-adherence, CS 0-1 means very low non-adherence. In addition, assessment of perception level, behavioral pattern, belief level and knowledge level of patients was also carried out with three questions for each. The three questions each on behavioral pattern and perception level were scored on a Likert spectrum scale, ranging from 0 to 4 score. Also, belief and knowledge level questions scaled from 0 to 4 score were used. Their cumulative scores were calculated and grouped into levels as follow:

i. Cummulative score for patient's perception towards medication and medical advice (PPP):

0 – 3 means Bad Perception (BP)

4 – 6 means Fair Perception (FP)

7 – 9 means Good Perception (GP)

10 – 12 means Excellent Perception (EP)

ii. Cummulative score for patient's behavioural pattern (PBP):

0 – 3 means Not Forgetful (NF)

4 – 6 means Rarely Forgetful (RF)

7 – 9 means Moderately Forgetful (MF)

10 – 12 means Highly Forgetful (HF)

iii. Cummulative score for patient's belief on medication (PBM):

0 – 3 means Worse Belief (WB)

4 – 6 means Bad Belief (BB)

7 – 9 means Good belief (GB)

10 – 12 means Excellent belief (EB)

iv. Cummulative score for patient's knowledge on medication and disease (PKM) has:

0 – 3 means Inadequate Knowledge (IK)

4 – 6 means Fair Knowledge (FK)

7 – 9 means Good Knowledge (GK)

10 – 12 means Excellent Knowledge (EK).

4.3 Medication Adherence Intervention Sub-System

Medication adherence intervention sub-system is a web-based application that provides secured and user-friendly platforms for Physician, Patient and Admin to carry out activities that support and improve medication adherence behaviour of patients and to help patients adhere to their prescribed medication. Such activities include but not limited to: simplification of medication dose and dosage during medication prescription by physician; composition and delivery of clinic appointment notification and reminder messages by Admin; medication and health information message alerts by Admin; delivery of patient-centric persuasive message centered on motivation, information, how to take medication, warning against risk of non-adherence to medication, counseling and so on via SMS and agent voice call. In addition, patients are provided with web portal and USSD code to access their prescription, appointment date and other health information capable of improving their wellness.

In order to develop an enhanced medication adherence intervention system, ANFIS predictive model, assessment of medication non-adherence sub-systems and adherence intervention sub-system are all interconnected and inter-related.

4.4 Use Case Diagram of the New System

A use case depicts a unit of functionality provided by the system. The use case diagram is a visual summary of a collection of several related use cases within the system that can be used to develop and visualize the user's active roles including the relationships among the actors (users) and the essential processes [44]. The proposed system has four classified users to include administrator, physician (doctor), patient and caregiver. In figure 3, the use case diagram of the proposed system which summarizes each identified user's functions with their inter-relationships and communications is shown. The main purpose of a use case diagram is to show what system functions are performed by which of the actors. It makes the analysis and design of new system to be simplified. Four actors are involved in the medication adherence intervention system. Specific roles of each actor including admin, physician, patient and caregiver in the system are presented in the use case diagram shown in figure 3. The patient use case depicts several functions of the patient which include; registration, book, view and cancel appointment, receive notification, search for information, report reactions and other enquiries. Use case that explains the activities that are carried out by the Doctor/Physician which include prescribe medication, book appointment, view appointment, and cancel appointment, response to drug reaction report, account maintenance, backup data and generate report are well represented.

5. RESULT AND DISCUSSION

The iMedicaIS is an intelligent machine learning prediction of medication non-adherence and intervention system for improving patient's adherence to medication. The system has three independent sub-systems which are integrated with web and mobile technologies to provide a unique and friendly web application for the end users to use. Each sub-system has its own design framework and implementation technologies. For example, the assessment of medication non-adherence sub-system was developed on ASP.Net framework and C#.Net with MS-SQL database. Web-based form was developed to serve as emulator which calculates medication non-adherence level of patient using Morisky medication adherence rating scale. The assessment emulator form displays 8-questions for the patient to answer and the responses are calculated and analysed and stored in the database as shown in Figure 4. In addition, the sub-system assesses the identified factors that influence patient's level of medication non-adherence which include belief, knowledge, perception and behavioural pattern. However, it is primarily meant for regular outpatients who have been taking the medication for some period of time.

In figure 5, an intelligent predictive model that can accurately predict level of medication non-adherence of patient was successfully developed using Adaptive Neuro-Fuzzy machine learning algorithm. It was implemented on Matlab R2020 programming environment. Four (4) most essential features or factors that influence medication non-adherence as inputs to the predictive model were extracted from the generated dataset of outpatients to build the predictive model as shown in figure 5.

From the figure 5, the model has four (4) input variables are perception, knowledge, behavioural pattern and belief and one (1) output variable which is non-adherence level. All the variables are fuzzified and their degrees of membership functions are defined with triangular and guassian membership functions. The generated non-clinical dataset of 609 records was partitioned into 70% and 30% for training and testing respectively. The ANFIS predictive model was developed and performed well on the non-clinical dataset containing patient's knowledge, belief, perception, behavioural pattern and medication non-adherence with the root mean square error (RMSE) being 0.391 and 0.416 in training and testing respectively. From the training and testing results, the system was able to accurately predict patients who are likely to be non-adherent and stratify the level of medication non-adherence and also provides the level of non-adherence to expect from the patient with high significant accuracy. The GUI implementation of the predictive model on Matlab is shown in figure 6.

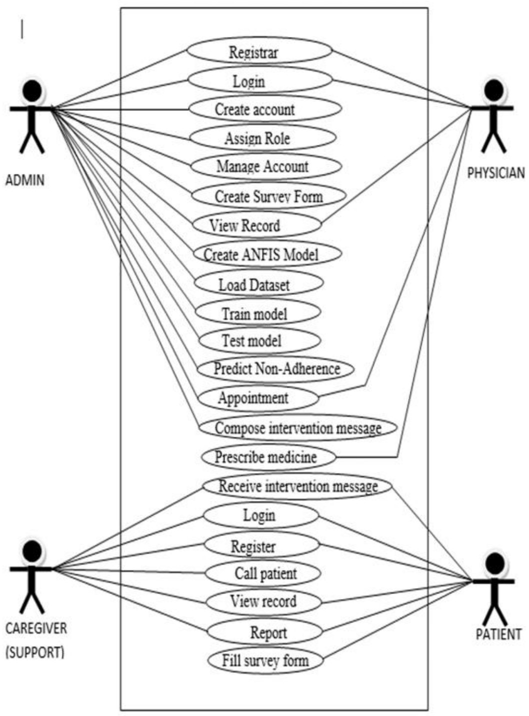

Figure 3. Use case diagram of iMedicaIS

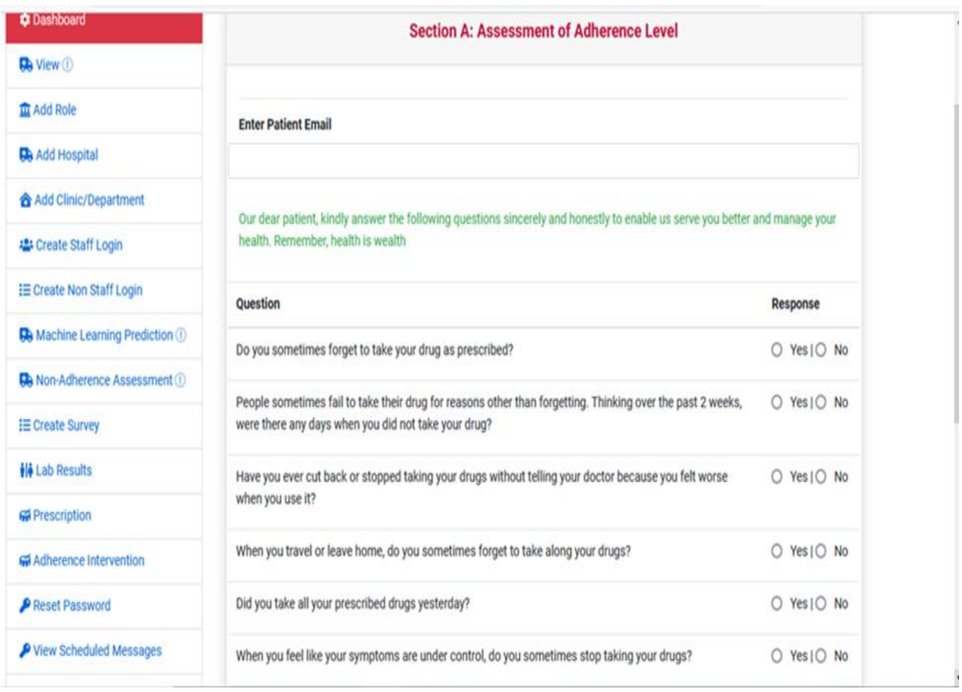

Figure 4. Assessment of medication adherence level form

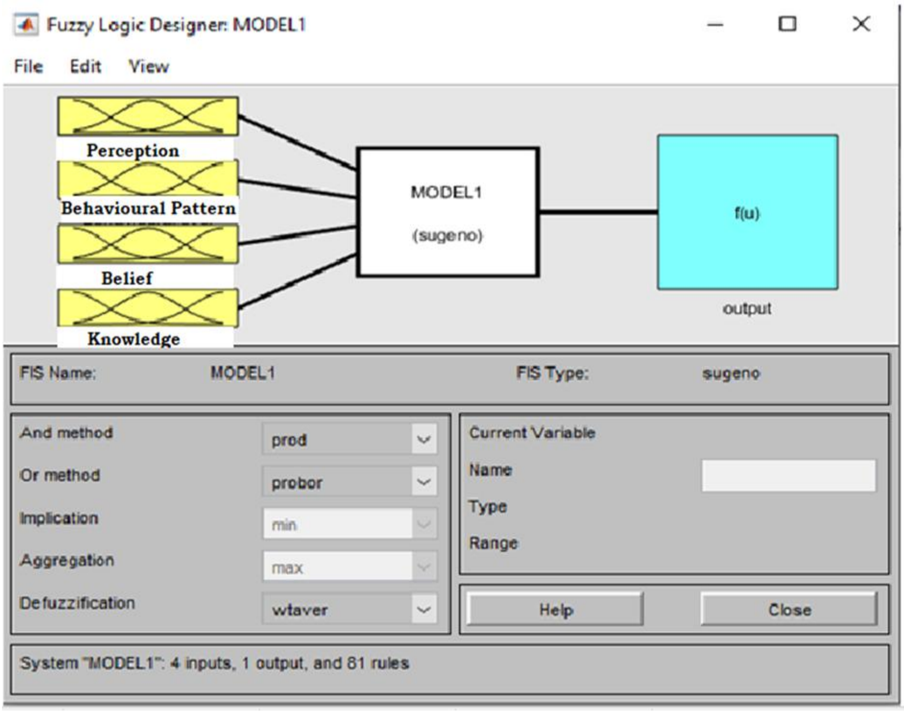

Figure 5. Implementation of ANFIS Predictive Model

Figure 6. Matlab Implementation of Medication Adherence

5.1 Sensitivity and Impact of the Input Variables on the Output Variables

There are two options to view the result of the ANFIS predictive model on Matlab programming environment which are rule viewer and surface viewer. Using the surface viewer, the degree of influence of input variables such as perception, knowledge, belief and behavioural pattern on the output variable which is non-adherence can be viewed in a three-dimensional (3D) graph. For examples, the relationship between knowledge level and behavioural pattern of patient towards non-adherence is shown in figure 7.

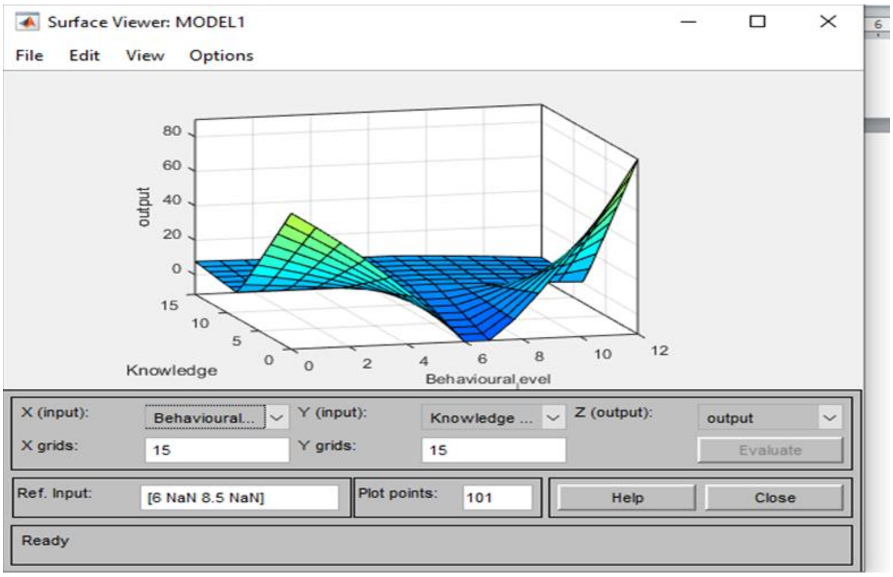

Figure 7. Correlation graph of knowledge and behavioural pattern towards non-adherence

From the figure 7, with the higher behavioural pattern level and knowledge level starting from 6.5 and 10 respectively give corresponding high medication non-adherence level that require adherence intervention. In addition, graphic user interface window for prediction of patient level of medication non-adherence was created to enable end user inputting the data and the system generated the non-adherence level of patient based on the inputted values. Outputs from the predictive model are used to drive the design and delivery of persuasive personalized adherence intervention activities such as medication prescription and composition of SMS and agent voice call information contents targeted towards individual patients. Finally, the adherence intervention sub-system of iMedicaIS combines both web and mobile phone technologies of Africa talking and Twilio APIs for end user's platforms implementation. The platforms enables medication prescription and clinical appointment, compose of adherence intervention persuasive messages and delivery of personalized persuasive messages via the integrated delivery tools such as SMS, voice agent call and USSD and web report.

5.2 System (iMedicaIS) performance evaluation

The iMedicaIS, is hybrid of three sub-systems consisting ANFIS predictive model, assessment of medication non-adherence sub-system and adherence intervention. It is evaluated by self-assessment through a comparative analysis with three selected relevant existing systems developed by the authors of MedAlert APP [45], Teen Path App [46] and predictive model [27]. The table 2 describes the comparison assessment of the three existing systems with iMedicaIS. All the selected predictive models reviewed in [27, 33, 35] when compared with the proposed iMedicaIS are limited to binary classification in their results and also failed to develop end user application driven by the results where caregivers and patients can be accommodated to use the system. The systems were analysed under three essential components of machine learning predictive model which are dataset, computational algorithms and result classification with performance metrics analysis.

1) Dataset: the quality and quantity of data values (features) in the dataset as variables are the most essential determinants. Predictive model efficiency, reliability and also its limitations depend on the dataset.

2) Computational algorithms: predictive models are usually based on soft computing algorithms that leverage on available dataset and its categorization to predict future outcomes. The computation algorithms used by authors in [27] and the iMedicaIS for predictive analytics are shown in the table 2. They include: logistic regression, backpropagation neural network, support vector machine, ensemble, fuzzy logic and adaptive neuro fuzzy inference system (ANFIS). However, all the above mentioned machine learning algorithms are

single based except the ANFIS used in this study which is hybrid thereby out-performed others.

3) Predictive model results are classified into two: binary and fuzzified or stratified.

From the comparative assessment in the table 2, the new system advanced in all the functions having integrated all the functions in each of the other three systems. Worthy of note is the predictive result classification which provides an in-depth insight to medication non-adherence level of patient through fuzzification. The patient's non-adherence is stratified into four levels to give better understanding and also to deploy appropriate intervention messages based on the individual patient's peculiar needs.

Table 2. Comparisons assessment

Features and Functions	**MedAlert App [45]**	**Teen Path App [46]**	**Wang *et al.*, (2020) Predictive Model [27]**	**iMedicaIS**
Supported platform	Web and mobile	Android mobile phone	Window	Web and mobile
GSM Supported	Yes	Yes	No	Yes
Dataset record	N/A	N/A	420	609
Input variables	N/A	N/A	4	4
Variable names	N/A	N/A	Belief, Attitude Knowledge and Depression with Anxiety	Belief, Behavioural Pattern, Knowledge Perception
Output variable	N/A	N/A	Non-adherence level	Non-adherence level
Predictive algorithm	Null	Null	Support vector machine, logistic regression and backpropagation neural network	Adaptive Neuro Fuzzy Inference System (ANFIS)
Non-adherence classification	Null	Null	Binary	Fuzzified
Assessment of non-adherence level	Null	Null	Yes	Yes
Delivery of adherence intervention	Yes	Yes	No	Yes
Delivery tool	SMS and voice call	SMS and voice call	No	SMS, agent voice call and USSD

6. Conclusion

By integrating medication non-adherence assessment system with ANFIS predictive model and adherence intervention system, a web based intelligent machine learning prediction of patient medication non-adherence level with intervention system named iMedicaIS has been developed. The system proffers solutions to the prevalent problem of medication non-adherence faced by outpatients especially those who require a long-time medication due to their chronic illness. The developed intelligent web-based application with integration of SMS, USSD and agent voice call API were implemented using Visual Studio Dot Net Framework, Matlab R2020a programming language, Twilio and Africa's Talking APIs and other web services. The adherence technological tools used to deliver personalize and persuasive adherence intervention messages to patients and other stakeholders for improving medication nadherence were SMS, agent voice call, web search and USSD. In addition, iMedicaIS has several modules and functions with capabilities to accurately identify patients who are unlikely to adhere to their prescribed medications and to deliver personalized persuasive messages as intervention. With the evaluation and usability results, the system has proven to be scalable, cost effective, simple to use and efficient in improving medication adherence.

References

[1] M. Julius, F. Onu, K. Okorie, U. Alo, C. Eze, G. Abanobi, "Multi-Dimensional Patients' Dataset for: Development of Online Assessment and Machine Learning Prediction of Medication Non-Adherence with Intervention System", Mendeley Data, V1, 2023. doi: 10.17632/3t39fctrzv.1

[2] S. J. Stewart, Z. Moon and R. Horne, "Medication nonadherence: health impact, prevalence, correlates and interventions", *Psychology and Health, 2023*; *38*(6), 726–765. Doi:10.1080/08870446.2022.2144923

[3] G. D. Chauke, O. Nakwafila, B. Chibi, B. Sartorius and T. Mashamba-Thompson, "Factors influencing poor medication adherence amongst patients with chronic disease in low-and-middle-income countries: A systematic scoping review," *Heliyon, Volume 8, Issue 6, 2022*, e09716, ISSN 2405-8440, https://doi.org/10.1016/j.heliyon.2022.e09716.

[4] A. Gast and T. Mathes, "Medication adherence influencing factors—an (updated) overview of systematic reviews," *Syst Rev* **8**, 112 (2019). https://doi.org/10.1186/s13643-019-1014-8

[5] K. Aikaterini and S. Stephen, "Reasons for Non-Adherence to Cardiometabolic Medications, and Acceptability of an Interactive Voice Response Intervention in Patients with Hypertension and Type 2 Diabetes in Primary Care: A Qualitative Study," *BMJ Open*, 2017;7:e015597. doi:10.1136/bmjopen-2016-015597.

[6] K. M. Kvarnstrom and L. Helena, "Barrier and facilitators to medication adherence: a qualitative study with general practitioners," *BMJ Open 2018*; 8:e015332. Doi:10.1136/bmjopen-2016-015332

[7] R. A. Atinga, L. Yarney and M. G. Narissa, "Factors Influencing Long-Term Medication Non-Adherence among Diabetes and Hypertensive Patients in Ghana: A Qualitative Investigation," *Plos One*, vol. 13, no 3, 2018.

[8] J. Xie, D. D. Zeng and Z. A. Marcum, "Using deep learning to improve medication safety: the untapped potential of social media," *TherAdv Drug Saf*, Vol. 8, no 12, pp. 375-377, 2017, 2017

[9] J. Car, W. S. Tan, Z. Huang, P. Sloot and B. D. Franklin, "eHealth in the Future of Medications Management: Personalisation, Monitoring and Adherence. *BMC Medicinem,* 2017, 15:73

[10] P.A. Aziah, W. M. Zahiruddin, S. MohdNazri, S. Sukeri, T. J. Tengku, R. A. Hamat, O.Malina, I. Norazlin, I. Zawaha, and A. W. Zainudin, "Knowledge, Attitudes, Practices and Beliefs Toward Leptospirosis among Urban and Rural Communities in Northeastern Malaysia", *International Environ. Research Public Health* 2018.15,2425 (2018).

[11] L. Ai-Hussany, S. Kloosterboer, B. Dierekx and B. C. Koch, "Assessing Methods of Measuring Medication Adherence in Chronically Ill Children – A Narrative Review," *Patient Preference and Adherence,* 2019: 13 1175-1189. (2019).

[12] D. Xu, W. Gong, S. Gloyd, E. D. Comic, J. Simon, J.P. Hughes, "Measuring adherence to anticipsychotic medications for schizophremia: Concordance and validity among a community sample in rural area," *PMC 2019.* https: 201:307-314 doi:10.1016/j.sch 2018.05.014

[13] R. I. Nassar, I. A. Basheti, and B. Saini, "Exploring Validated Self-Reported Instruments to Assess Adherence to Medications Used: A Review Comparing Existing Instruments," *Patient Prefer Adherence*, vol. 16, pp. 503-513, Feb., 2022. doi:10.2147/PPA.S352161

[14] E. Crayton, A. J. Wright and M. Ashworth, "Improving Medication Adherence in Stroke Survivors: Intervention Development Process," *BMC Health Service Research*, vol. 18, no. 1, pp. 772 - 785. Https://doi.org/10.1186/s12913-018-3572-1. (2018).

[15] B. Sleath, S. J. Blalock, D. M. Carpenter, R. Sayner, K. W. Muir, C. Slota, S. D. Lawrence, A. L. Giangiacomo, M. E. Hartnett, G. Tudor, J. A. Goldsmith, and A. L. Robin, "Ophthalmologist-patient Communication, Self-efficacy, and Glaucoma Medication Adherence," *Ophthalmology*, vol. 122, no. 4, pp. 748-754. doi: 10.1016/j.ophtha.2014.11.001 (2015).

[16] A. J. Cross, R. A. Elliott, K. Petrie, L. Kuruvilla, J. George, "Interventions for improving medication-taking ability and adherence in older adults prescribed multiple medications," *Cochrane Database Syst Rev*. Vol. 5, no. 5, 2020. CD012419. Published 2020 May. doi:10.1002/14651858.CD012419.

[17] B. Jimmy, J. Jose, "Patient medication adherence, measures in daily practice," *Oman Med J*. vol. 26, no. 3, pp. 155-159, 2011. doi:10.5001/omj.2011.38

[18] E. Costa, A. Giardini, M. Savin, E. Menditto, E. Lehane, O. Laosa, S. Pecorelli, A. Monaco and A. Marengoni, "Interventional tools to improve medication adherence: review of literature," *Patient Preference and Adherence*, vol. 9, pp. 1303-1314, Sept., 2015

[19] S. Hamtaeigashti, M. Shamsi, M. A. Sahraian, R. S. and A. Almasi-Hashiani, "Effect of an educational intervention based on the theory of planned behavior on improving medication adherence in patients with multiple sclerosis treated with injectable disease-modifying drugs: randomized controlled trial," *BMC Public Health (2023) 23:999* https://doi.org/10.1186/s12889-023-15910-6

[20] R. Orji and R. Maffath, "Persuasive Technology for Health and Wellness State-of–the Art and Emerging Trends," *Health Informatics Journal*, vol. 24, no. 1, pp. 66 – 91. (2018).

[21] K. T. Win, J. Mullan, S. Howard, and H. Oinas-Kukkonen, "Persuasive Systems Design Features in Promoting Medication Management for Consumers," *University of Wollongong Research Online*, https://ro.uow.edu.au/eispapers1?utm_source=ro.uow.edu.au%2Feispapers1%2F381&utm_medium=PDF&utm_campaign=PDFCoverPages, Jan., 2017

[22] S. Tran, L. Smith, S. El-Den, and S. Carter, "The Use of Gamification and Incentives in Mobile Health Apps to Improve Medication Adherence: Scoping Review," *JMIR Mhealth Uhealth*, vol. 10, no. 2, 2022, e30671.URL: https://mhealth.jmir.org/2022/2/e30671. DOI: 10.2196/30671

[23] T. Fritz, G.C. Murphy and T. Zimmermann, "Persuasive Technology in the Real World". A Study of Long-Term Use of Activity Sensing Devices for Fitness," *CHI '14: Proceedings of the SIGCHI Conference on Human Factors in Computing Systems*, pp. 487 - 496, 2014, https://doi.org/10.1145/2556288.2557383

[24] F. S. Lopez and N. Condori-Fernandez, "Design of an Adaptive Mobile Application for Simulating the Medication Adherence," *ICST Institute for Computer Sciences, Social Informatics and Telecommunications Engineering, 2017. ENICST178*, pp. 99-105. DOI: 10.1007/978-3-319-49616-0-9 (2017).

[25] R. Cialdini, "Influence: Science and Practice." *Allyn and Bacon*, Boston, 2001.

[26] X. Wu, Y .M. Choi, and M. Ghovanloo, "Design and Fabricate Neckwear to Improve the Elderly Patients' Medical Compliance" *in Proceedings of the International Conference on Human Aspects of IT for the Aged Population*, Los Angeles, CA, USA, 2-7, pp. 222-2354 (2015).

[27] L.Wang, F. Rong, Z. Cheng, H. Liwen, Z. Tianyu, C. Ying, L. Kai, W. Zhengting and Z. Jie, "Applying Machine Learning Models to Predict Medication Non-Adherence in Crohn's Disease Maintenance Therapy." *Patient Preference an Adherence*:14 917-926. (2020).

[28] M. S. Julius, U. R. Alo, F. U. Onu, and C. I. Akobundu, "Machine Learning Framework to Predict Non-adherence to Medication using Non-clinical Data: A Prognosis Approach," Proceedings of the 9th International Conference on Computer and Communications Management, pp. 98-103. July, 2021

[29] M. S. Julius, U. R. Alo, F. U. Onu, C. I. Akobundu, C. O. Agwu, N. H. Ogbu, and F. C. Eze, "Cloud-based Medication Non-adherence Assessment and Intervention System," International Congress on Information and Communication Technology, pp. 647-658, Feb, 2024.

[30] K. Akyol, "Coronary Artery Disease Classification With Support Vector Machine Tuned via Randomized Search Cross-Validation," *Research Square*.

Https://doi.org/10.21203/rs.3.rs-1551634/vi. (2022).

[31] H. O. Alanazi, A. H. Abdullah, K. N. Qureshi, and A. S. Ismail, "Accurate And Dynamic Predictive Model for Better Prediction In Medicine and Healthcare," *Ir J Med Sci,* 187, pp. 501-513 (2018).

[32] D. Bzdok and A. Meyer-lindenberg, "Machine Learning for Precision Psychiatry: Opportunities and Challenges. Biological Psychiatry:" Congnitive Neuroscience and Neuroimaging, vol. 3, no. 3, pp. 223-230. (2018).

[33] Y. Gu, A. Zalkikar, M. Liu, L. Kelly, A. Hall, K. Daly and T. Ward, "Predicting Medication Adherence Using Ensemble Learning And Deep Learning Models With Large Scale Healthcare Data." *Scientific Reports:* Https://doi.org/10.1038/s41598-021-98387-w. (2021).

[34] T. Janssoone, "Machine Learning on electronic health records: models and features usages to predict medication non-adherence". *ArXiv preprint*:1811.12234. (2018).

[35] C. Mohite, "Leveraging Machine Learning Framework to Predict Buprenorphine/Naloxone Treatment Discontinuation," *Northern University Boston Massachusetts*. (2020).

[36] M. Zhou, Y. Fokuoka, K. Goldberg, E. Vittinghoff, and A. Aswani, "Applying machine learning to predict future adherence to physical activity programs," *BMC Medical Informatics and Decision Making:* 19.69 (2019).

[37] P. Shashank, A. Jahnavi, and M. Sujatha, "Predicting Emergency Department Services in Hospital Using Machine Learning," *IOSR Journal of Computer Engineering*, vol. 21, no. 2, pp. 15-22 (2019).

[38] A. Yadollahpour, J. Nourozi, S. Mirbagheri, Simancas-Acevedo, E. and F. Trejo-Macotela, "Designing and Implementing an ANFIS Based Medical Decision Support System to Predict Chronic Kidney Disease Progression," *Frontiers in Physiology,* vol. 9, Article 1753. (2018).

[39] K.D. Magano, A.M. Kurien, and A. Chibani, "Fuzzy Based Diagnostic Agent for Context Aware Patient Monitoring," *The 8th International Conference on Current and Future Trends of International and Communication Technologies in Healthcare, Proceedia Computer Science*, vol. 141, pp. 421-427 (2018).

[40] S. Zhang, Y. Yuan, Z. Yao, X. Wang, Z. Lei, "Improvement of the Performance of Models for Predicting Coronary Artery Disease Based on Xgboost Algorithm and Feature Processing Technology," *Electronics MDI*. 11, 315. https://doi.org/ 10.3390/electronics11030315. (2022).

[41] S. K. Sahoo and S. S. Goswami, "A Comprehensive Review of Multiple Criteria Decision-Making (MCDM) Methods: Advancements, Applications, and Future Directions," *Decision Making Advances*, vol. 1, no. 1, pp. 25–48, Jun. 2023.

[42] C. M. U-Dominic, J. C. Ujam, and N. Igbokwe, "Applications of Analytical Hierarchy Process (AHP) and Knowledge Management (KM) Concepts in Defect Identification: A Case of Cable Manufacturing", *Asian J. Adv. Res. Rep.*, vol. 15, no. 5, pp. 9–21, Aug. 2021.

[43] A. A. Egwor, E. A. Onibere, and P. O. Odion, "Application of neuro-fuzzy system: a literature review,*" International Journal of Computer Science and Network Security*, vol. 18, no.12, 2018

[44] H. J. Rosenblatt, "System analysis and design," *Tenth Edition course technology. Shelly cashman services*, 2014.

[45] R. S. Okuboyejo and O. K. Eyesan, "Design and implementation of a voice-based medical alert system for medication adherence," Procedia Technology, pp. 1035-1040, 2013.

[46] D. A. Shellmer, M. A. Dew, G. Mazariegos, and D. A. DeVito, "Development and field testing of Teen Pocket PATH, a mobile health application to improve medication adherence in adolescent solid organ recipients", *Pediatric Transplantation, Published by John Wiley & Sons Ltd* 2016.